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                 CAS definition of basic patents expanded to ensure
                 comprehensive access to substance and sequence
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         SEP 25
                 CA/CAplus current-awareness alert options enhanced
                 to accommodate supplemental CAS indexing of
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- L4 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
- AN 2005617411 MEDLINE
- DN PubMed ID: 16186108
- TI Tyrosine 740 phosphorylation of discoidin domain receptor 2 by Src stimulates intramolecular autophosphorylation and Shc signaling complex formation.
- AU Yang Kyungmi; Kim Jeong Hak; Kim Hae Jong; Park In-Sung; Kim Ick Young; Yang Beom-Seok
- CS Biomedical Research Center, Korea Institute of Science and Technology, 39-1, Hawolgok-Dong, Sungbuk-Ku, Seoul 136-791, Korea.
- SO The Journal of biological chemistry, (2005 Nov 25) Vol. 280, No. 47, pp. 39058-66. Electronic Publication: 2005-09-26. Journal code: 2985121R. ISSN: 0021-9258.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
- LA English
- FS Priority Journals
- EM 200602
- ED Entered STN: 22 Nov 2005
 Last Updated on STN: 3 Feb 2006
 Entered Medline: 3 Feb 2006
- DDR2 is a receptor tyrosine kinase whose activating AΒ ligands are various collagens. DDR2-mediated cellular signaling has been shown to require Src activity. However, the precise mechanism underlying the Src dependence of DDR2 signaling is unknown. Here, using baculoviral co-expression of the DDR2 cytosolic domain and Src, we show that Src targets three tyrosine residues (Tyr-736, Tyr-740, and Tyr-741) in the activation loop of DDR2 for phosphorylation. This phosphorylation by Src stimulates DDR2 cis-autophosphorylation of additional tyrosine residues. In vitro Shc binding assays demonstrate that phosphotyrosines resulting from DDR2 autophosphorylation are involved in Shc binding to the DDR2 cytosolic domain. Mutating tyrosine 740 of DDR2 to phenylalanine stimulates autophosphorylation of DDR2 to an extent similar to that resulting from Src phosphorylation of DDR2. In addition, the DDR2 Y740F mutant protein displays collagen-independent, constitutively activated signaling. These findings suggest that tyrosine 740 inhibits DDR2 autophosphorylation. Collectively, our findings are consistent with the following mechanism for Src-dependent DDR2 activation and signaling: 1) ligand binding promotes phosphorylation of Tyr-740 in the DDR2 activation loop by Src; 2) Tyr-740 phosphorylation stimulates intramolecular autophosphorylation of DDR2; 3) DDR2 autophosphorylation generates cytosolic domain phosphotyrosines that promote the formation of DDR2 cytosolic domain-Shc signaling complexes.